## Peer Review File

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## <mark>Reviewer A</mark>

A small correction in Line-87: 18 years of age.

**Reply:** We firstly thank the reviewer for the proposal. We have modified our text as advised (see Page 5, line 87).

## <mark>Reviewer B</mark>

The epidemiological study on patients with pulmonary embolism (PE) with regards to pulmonary infarction (PI) was quite intriguing. According to Chest (1991;100(3):598), about 10% of these patients develop small thrombi that lodge distally into the segmental and subsegmental vessels, resulting in a pulmonary infarction. These patients often present with symptoms like pleuritic chest pain and hemoptysis, which are believed to be due to an intense inflammatory response in the lungs and adjacent visceral and parietal pleura.

However, for a more impactful publication, it would be ideal to present novel insights. Specifically:

Clinical Implications:

1. How does the diagnosis of PI change the management of such patients?

**Reply 1:** We firstly thank the reviewer for the proposals. PI may be an important diagnostic clue or even the only sign of acute PE. The diagnosis of PI reduced missed and misdiagnosed pulmonary embolism and avoided delayed diagnosis. These patients received anticoagulant or thrombolytic therapy as soon as possible. In addition, non-steroidal anti-inflammatory drugs could be administered to alleviate severe chest pain in patients with PE and PI. There were no other special treatments available. The management of PI patients followed the guidelines of PE. We added these contents (see Page 11, line 220-223). We added some data on treatment (see Table 1). There was no difference between the two groups in anticoagulation and thrombolysis.

2. Can differentiation between fever plus consolidation and conditions like pneumonia, tuberculosis, and invasive fungal infection be made? Could this potentially prevent unnecessary antibiotic use?

**Reply 2:** We thank the reviewer for the very valuable advices. The consolidation is not specific to PI, because it can also observed in pneumonia, tuberculosis, and invasive fungal infection. The internal morphologic characteristics of consolidation could be differentiated from other causes. Reversed halo sign (RHS) is a typical sign of PI. PI is a peripheral wedge-shaped consolidation with central lucencies, low-attenuation areas (with or without reticulation), vessel sign, and the absence of air bronchograms. And PI is more common in the lower lobes. Typical chest CT findings for pneumonia are patchy consolidations with air bronchograms. Tuberculosis is frequently accompanied by tree-in-bud sign and nodules. Reticulation inside the RHS halo is also very common in invasive fungal infection(IFI). It should be interpreted with consideration of the overall clinical presentation and the patient's immune status. In an immunocompromised patient, the RHS with reticulation is highly suggestive of IFI. With increasing awareness and improved diagnosis of PI, the rate of the misdiagnosis decreases, and this can potentially prevent unnecessary antibiotic use. In our study, 25% of PI patients applied antibiotics. We added these contents (see Page 9-10, line 179-191).

Clinical Outcome:

Does diagnosing PI change management?

**Reply:** We thank the reviewer for the comment. PI is a complication of pulmonary embolism and does not change management. We added these contents (see Page 11, line 220-221).

Are there any differences in hospital stay duration and mortality between the two groups?

**Reply:** We firstly thank the reviewer for the proposals. There was no obvious difference in hospital stay duration(10.5 vs 10, P=0.412) and mortality(0 vs 2, P=1.000) between the two groups(see Page 7, line 136-137). The sample size is comparatively limited. In the future, we will increase the sample size of pulmonary infarction, there may be different results.

Should we be prepared for intubation due to hemoptysis?

Reply: We thank the reviewer for the suggestion. Pulmonary embolism often caused a small amount of

hemoptysis, which was usually treated symptomatically. However, in the case of severe hemoptysis, it can be quite challenging. If massive dyspnea has not been relieved or hypoxia has been aggravated, tracheal intubation should be done immediately to keep the respiratory tract open. In our study, patients with pulmonary embolism did not experience massive hemoptysis. We added these contents (see Page 11-12, line 223-227).

Would admission to the ICU or ventilation support be necessary?

**Reply:** We agree with the reviewer's comments. High-risk patients with hemodynamic instability, including cardiac arrest, obstructive shock, or persistent hypotension should be immediately admitted to the relevant intensive care unit. We added these contents (see Page 12, line 227-230).

While the physical findings utilized are already known as per Thromb Res (2021 Jun;202:162-169), we would need clarifications on:

Definition of Recent Trauma: Does this refer to events like a femoral neck fracture leading to the risk of fatal embolism? Or prolonged bed rest leading to DVT? Or does it causes chest injury directed to the trauma of the lung? The confounding factors seem manifold.

**Reply:** The reviewer is right. Recent trauma refers to lower limb injuries such as femoral neck fractures, patellar fractures, etc. that result in recent bed rest. It does not lead to a fatal embolism. We have modified our text as advised (see Page 3, line 102-103).

Exclusion Criteria: Why were individuals diagnosed via V/S excluded?

**Reply:** We thank the reviewer for the comments. In ventilation-perfusion scintigraphy (V/Q scan), the main signs are well-defined pulmonary lobe and segmental perfusion defects. But the specific location of pulmonary artery thromboembolism cannot be observed. In our study, it is necessary to observe embolism locations, so we excluded individuals diagnosed via V/S. We added these contents (see Page 5, line 90-92).

Multivariate Analysis: It would enhance readability if significant factors in the multivariate analysis are highlighted in bold.

**Reply:** We thank the reviewer for the proposals. The significant factors in the multivariate analysis have been highlighted in bold (see Table 4).

Age as a Significant Factor: Though emphasis is placed on age being significant, with an ODD ratio of 0.975, the risk difference is a mere 2.5%. Figure 2 appears to suggest that younger individuals have a higher risk of PI. However, is this in the context of PI/PE with PI or PI/all PE? Given the retrospective study, if the age distribution of PE patients isn't shown in the table, it may lead to potential misinterpretation. For instance, the hospital might predominantly admit younger patients.

**Reply:** We thank the reviewer for the comments. Age was a protective factor in the multivariate analysis. The odds ratio (OR) of gender is 0.975, which means that when age increases by one unit, pulmonary infarction decreases by 0.975 times. This is consistent with the viewpoint expressed in Figure 2, that younger individuals have a higher risk of PI. The percentage in Figure 2 represents the ratio of pulmonary infarction to pulmonary embolism patients in each age group. We added the age distribution of PI and PE patients to avoid misinterpretation (See Figure 2A). In addition, the hospital mainly treats patients based on the risk level of pulmonary embolism and does not select patients based on age.